

# Free-Radical Chemistry of Sulfite

by P. Neta\* and Robert E. Huie\*

The free-radical chemistry of sulfite oxidation is reviewed. Chemical transformations of organic and biological molecules induced by sulfite oxidation are summarized. The kinetics of the free-radical oxidations of sulfite are discussed, as are the kinetics of the reactions of the sulfite-derived radicals  $\dot{\text{S}}\text{O}_3$  and the peroxy derivative  $\text{SO}_3$  with organic compounds.

Sulfur dioxide is a major air pollutant, formed primarily during the combustion of fossil fuels. Other sources include natural gas scrubbing, the oxidation of naturally emitted reduced sulfur compounds, and smelting of sulfide ores (1). Sulfur dioxide is water-soluble, forming bisulfite and sulfite



and at very high concentration, disulfite.



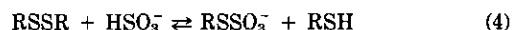
At any physiological pH, sulfite and bisulfite will both be important forms of S(IV). We will use primarily the term sulfite to refer to the equilibrium mixture, except when referring specifically to bisulfite. The term S(IV) will be used to include other compounds containing sulfur in the +4 oxidation state.

Sulfur dioxide can produce bronchoconstriction upon inhalation, particularly in asthmatics and during exercise (5,6). In addition to inhalation of  $\text{SO}_2$ , sulfite can enter the body due to its use as a preservative in food, wine, and medications. Finally, sulfite is a likely intermediate in the metabolism of sulfur containing amino acids such as methionine and cysteine.

Both liver and lung tissues contain the enzyme sulfite oxidase which catalyzes the oxidation of sulfite to sulfate. This has led to two contrary views of the possible physiological consequences of ingested sulfite. One point of view is that the body contains sufficient sulfite oxidase to detoxify any reasonably likely dose of sulfite from either inhaled atmospheric  $\text{SO}_2$  or from food additives (7). The other view is that sulfite reaches the blood and forms S-sulfocysteine,  $\text{RSSO}_3^-$  and, therefore, the sub-

sequent chemistry of S(IV), at least as the S-sulfocysteine, must be considered (8). Further, epidemiological evidence suggests a relation between  $\text{SO}_2$  and lung cancer in workers exposed to arsenic and animal studies on benz(a)pyrene correlate cancer development with  $\text{SO}_2$  exposure (8).

Sulfite is a strong nucleophile and reacts with many biomolecules by substitution at electrophilic positions. These reactions have been reviewed by Petering (8) and will not be discussed here, other than the reaction of bisulfite with cystine [Eq. (4)].



This reaction has an equilibrium constant of 0.089 at pH 7.75 and 37°C (9). The large concentration of RSSR causes most sulfite in the blood to be bound as S-sulfocysteine,  $\text{RSSO}_3^-$ . As Petering points out, the biochemistry of  $\text{HSO}_3^-$  becomes the biochemistry of  $\text{RSSO}_3^-$  beyond the lung.

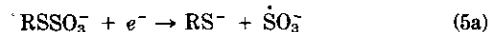
Because of the above equilibrium, however, S-sulfocysteine may act as a reservoir for sulfite; when it reaches cells in which RSH is in greater abundance than RSSR, e.g., liver cells, where  $\text{RSH}:\text{RSSR} = 10^2\text{--}10^3$  (10), the equilibrium may shift to the left to produce sulfite.

The present review deals exclusively with elements of the radical chemistry of sulfite. In light of the discussion above, it might appear that radical reactions initiated by sulfite are likely to be unimportant. There are, however, two possible sources of radicals from sulfite that can be considered.

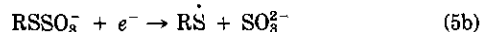
First, the lung and the rest of the respiratory system, being rich in oxygen, provide an environment for the autoxidation of sulfite before it can either be removed by sulfite oxidase or converted to S-sulfocysteine. The autoxidation of sulfite may be initiated by trace metal ions or certain enzymes and clearly involves free radicals (11,12). The second possible source of radicals is

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from *S*-sulfocysteine. The one-electron reduction of  $\text{RSSO}_3^-$  can be written as either



or



Pulse radiolysis experiments in which cysteine radicals were produced in the presence of  $\text{SO}_3^{2-}$ , or in which  $\text{SO}_3^-$  radicals were produced in the presence of cysteine, showed that RS oxidizes sulfite and that, therefore, the first path is more likely.

## Chemical Transformations Induced by Sulfite Oxidation

Much of the interest in the chemistry of radicals derived from sulfite arises from the observations that the reaction of sulfite with several organic compounds requires the presence of an oxidizing agent, usually molecular oxygen. Complementary to these observations are the many studies that show that certain organic compounds inhibit the oxidation of sulfite by oxygen.

The investigation of the effects of organic substances on the rate of oxidation of sulfite solutions by oxygen was initiated by Bigelow (13) and carried on actively for several years (14,15). In the work involving the oxidation of sulfite catalyzed by trace metal ions, the inhibition could have been caused by the complexation of the metal ion. Therefore, studies were carried out in which sulfite oxidation was initiated by ultraviolet light (16). Again, organic substances were found to inhibit the reaction. The photochemical reaction was shown subsequently to be a chain reaction and the inhibition by organic compounds due to breaking the free-radical chains.

Since the inhibition of sulfite oxidation involves, in general, only small total amounts of reaction, products of the chain breaking reaction usually have not been discussed. Also, in some cases the initial reactant might be regenerated in a secondary process. In other cases, however, the chemical transformation of the inhibitor was evident. This was observed initially for quinine sulfate and pyridine, which turned green, and hydroquinone, which became opalescent (16). Other work showed that the inhibition of sulfite oxidation by alcohols was accompanied by their oxidation (17). In subsequent work, the oxidation of sulfite in the presence of unsaturated compounds was found to result in the addition of sulfite to double bonds (18). With pyridine this leads to formation of *N*-pyridinium sulfonate (19). The reaction of hydroquinone with sulfite in the presence of oxygen is perhaps the most studied (20,21), since sulfite was used as a preservative in hydroquinone-based photographic developers (22). In this system two types of reaction appear to take place: (a) oxidation of the hydroquinone by sulfite radicals and by molecular oxygen, and (b) sulfonation of the quinone to form hydroquinone

sulfonates (followed by oxidation of the latter to quinone sulfonates) (21).

From the point of view of this review, the most important observations have been on the transformation of biological molecules by sulfite in the presence of oxygen. Fridovich and Handler (23) have shown that a mixture of horseradish peroxidase, hydrogen peroxide, and a peroxidizable substance initiate sulfite oxidation. Indeed, they used the oxidation of sulfite as a sensitive test for the production of radicals in biological systems (24). Klebanoff (25) confirmed this finding and further reported that the oxidation of NADH by  $\text{Mn}^{2+}$ , peroxidase, and  $\text{O}_2$  was stimulated by sulfite. Therefore, a biological system can initiate the oxidation of sulfite and the subsequent chain reaction can provide reactive intermediates capable of reacting with biological molecules.

Since this early work, there have been several papers on the oxygen induced reactions of biological molecules with sulfite. It has been found that oxygen is required for the complete sulfonation of protein S-H groups by sulfite (26). Sulfite was found to form sulfonates with 4-thiouracil derivatives in the presence of oxygen and this reaction was observed to be inhibited by hydroquinone (27,28). Methionine has been shown to be oxidized to the sulfoxide in the presence of sulfite,  $\text{O}_2$ , and  $\text{Mn}^{2+}$  (29). This reaction appears to be inhibited by superoxide dismutase. Sulfite cleaves DNA in the presence of  $\text{O}_2$  and  $\text{Mn}^{2+}$  (30), this reaction is inhibited by hydroquinone. The autooxidation of sulfite can destroy indole-3-acetic acid (31) or tryptophan (32) and several nucleotides and nucleic acids have been shown to react with sulfite in the presence of oxygen (33).

Lipid peroxidation has been induced by sulfite (34). This reaction is not only quenched by an antioxidant, 2,6-di-*tert*-butyl-4-hydroxymethylphenol, but also by  $\text{Mn}^{2+}$ . This suppression of lipid peroxidation by  $\text{Mn}^{2+}$  has also been observed in rat liver homogenate (35). Both  $\beta$ -carotene (36) and vitamin B1 (37) are destroyed during the autooxidation of sulfite. Finally, papain is inactivated during sulfite autooxidation in a reaction which leads to the incorporation of sulfite into the protein (38).

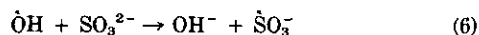
In this review, we will discuss the chemistry of the free radicals  $\dot{\text{SO}}_3^-$  and  $\text{SO}_5^-$ , key intermediates formed in the autooxidation of sulfite. In addition, we will discuss briefly the radicals  $\dot{\text{SO}}_2^-$  and  $\text{SO}_4^-$  and the ion  $\text{HSO}_5^-$ , due to their possible relationship to the behavior of sulfite in the body.

## Formation and Detection of $\dot{\text{SO}}_3^-$ Radicals

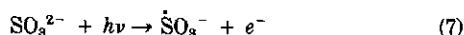
The sulfite radical is generally produced by the one-electron oxidation of sulfite or bisulfite ions, either chemically or photolytically. The radical is detected either by ESR or by optical absorption spectroscopy. Although the ESR detection is more definitive, kinetic studies on the sulfite radical are more often carried out by absorption spectroscopy, by monitoring either the

absorption of  $\dot{\text{SO}}_3^-$  itself or more frequently by following the formation of other more strongly absorbing species arising from  $\text{SO}_3^-$  reactions with substrates.

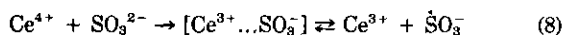
The  $\text{SO}_3^-$  radical has been produced by oxidation of sulfite with  $\text{Ce}^{4+}$  in acid solution (39–41), by reaction of sulfite with radicals produced by Fenton-type reagents, e.g.,  $\dot{\text{OH}}$ ,  $\text{NH}_2$ , and  $\text{SO}_4^-$  (from the reaction of  $\text{Ti}^{3+}$  with  $\text{H}_2\text{O}_2$ ,  $\text{NH}_2\text{OH}$ ,  $\text{S}_2\text{O}_8^{2-}$ , respectively) (42), by reaction with radiolytically produced  $\dot{\text{OH}}$  radicals or other oxidizing radicals (43–47)



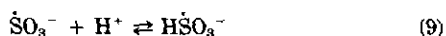
by photoionization of sulfite directly (3,48,49) or through photosensitizers (49)



or by photolysis of dithionate (50) or thiosulfate (51). The  $\text{SO}_3^-$  single-line ESR spectrum has been detected by using all of the above techniques (39–42,46,47,49,51), as well as in biochemical systems such as horseradish peroxidase–hydrogen peroxide (52) or prostaglandin hydroperoxidase (53). Most of these studies reported a  $g$  factor for  $\text{SO}_3^-$  around 2.0030, except experiments with  $\text{Ce}^{4+}$  in acid solutions, where  $g = 2.0022$  has been measured (39–41). This difference may suggest a possible complexation of  $\text{SO}_3^-$  with  $\text{Ce}^{3+}$ .

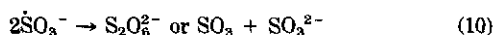


The alternative explanation that the  $g$ -factor shift is due to protonation of the radical



appears unlikely, since the  $\text{Ce}^{4+}$  experiments were carried out at  $\text{pH} \leq 2$ , while radiolytic and photolytic experiments showed no  $g$ -factor shift between  $\text{pH} 0$  and  $\text{pH} 12$  (49,54). The unpaired spin on  $\text{SO}_3^-$  has been calculated to be 62% on the sulfur and 13% on each of the oxygens (55,56).  $\text{SO}_3^-$  can be considered, therefore, as a sulfur-centered radical.

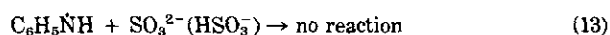
The optical absorption of  $\dot{\text{SO}}_3^-$  exhibits  $\lambda_{\text{max}} = 255$  nm with  $\epsilon_{\text{max}} = 1000 \text{ M}^{-1} \text{ cm}^{-1}$  (48). This relatively weak UV absorption has been used to determine the second-order decay rate constant for this radical



( $2k = 1.1 \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}$ ) (3,44,49) but is not conveniently used for following the kinetics of  $\text{SO}_3^-$  reactions with substrates since many of these substrates or their radical products mask the  $\text{SO}_3^-$  UV absorption. Therefore, in pulse radiolysis experiments often the absorption of the other substrate radical was monitored.

## Kinetics of One-Electron Oxidation of Sulfite

As mentioned above, sulfite or bisulfite ions undergo one-electron oxidation by several radicals to produce  $\text{SO}_3^-$ . Rate constants for a number of reactions of this type have been determined by pulse radiolysis and are summarized in Table 1. The hydroxyl radical reacts with both sulfite and bisulfite with very high rate constants, near the diffusion-controlled limit. The rate of oxidation by other radicals decreases in an order that appears to reflect the order of expected oxidation potentials of these radicals. Measurements of rate constants over a wide range of pH allows the separate determination of rate constants for the oxidation of sulfite and bisulfite. Whereas the hydroxyl and sulfate radicals react with bisulfite about twice as fast as with sulfite, for every other radical the reaction with sulfite is the faster by far. For  $\text{Br}_2^-$  the ratio is about 4; for the weaker oxidant  $\text{I}_2^-$ , the ratio is about 200. For the dimethylaniline radical cation, the reaction with sulfite is very fast ( $9.9 \times 10^8 \text{ M}^{-1} \text{ sec}^{-1}$ ) while the reaction with bisulfite is too slow to measure, ( $< 8 \times 10^5 \text{ M}^{-1} \text{ sec}^{-1}$ ). Similarly, the aniline radical cation  $\text{C}_6\text{H}_5\text{NH}_2^+$  oxidizes  $\text{SO}_3^{2-}$  with  $k = 4 \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}$  and  $\text{HSO}_3^-$  much more slowly,  $k = 4.8 \times 10^6 \text{ M}^{-1} \text{ sec}^{-1}$ .



The neutral aniline radical,  $\text{C}_6\text{H}_5\dot{\text{N}}\text{H}$ , on the other hand, does not oxidize sulfite. The cation radicals from promethazine, tryptophan, and tryptamine also oxidize  $\text{HSO}_3^-$  with moderate rate constants (Table 1) and in these cases the reactions were found to lead to equilibrium. The reverse reactions and equilibrium constants will be discussed below.

Since the autooxidation of sulfite solutions was found to be catalyzed strongly by trace amounts of transition metal ions, the reactions of sulfite with metal ions in their higher oxidation states has been the subject of many studies (11). Frequently, these studies are complicated by the ability of sulfite to complex these metal ions. These complexes are often quite stable; mercuric ion (in the presence of chloride) is used to protect sulfite from air oxidation (67). Other metal ion-sulfite complexes are more labile, decomposing presumably to the reduced metal ion and the sulfite free radical. For strong oxidants like  $\text{Mn(III)}$ , the reaction is fast and apparently irreversible (68). For weaker oxidants like  $\text{Fe(III)}$ , the reaction is much slower and reversible, making the derivation of an elementary rate constant for the oxidation of sulfite difficult.

For substitution-inert metal ion complexes, the situation is somewhat simpler since complex formation by sulfite is not important. Rates have been measured for the reactions of several metal ion complexes and rate

Table 1. Rate constants for reactions of sulfite with radicals.

Reaction	pH	$k$ , $M^{-1} \text{sec}^{-1}$	Reference
$\text{OH} + \text{HSO}_3^-$	—	$9.5 \times 10^9$	(57)
$\text{OH} + \text{SO}_3^{2-}$	—	$5.5 \times 10^9$	(57)
$\text{O}^- + \text{SO}_3^{2-}$	14	$3 \times 10^8$	(43)
$\text{O}_2^- + \text{SO}_3^{2-}$	9.8	82	(45)
$\text{SO}_4^- + \text{HSO}_3^-$	—	$\geq 1 \times 10^9$	(3)
$\text{SO}_4^- + \text{SO}_3^{2-}$	—	$\geq 5 \times 10^8$	(3)
$\text{SO}_4^- + \text{HSO}_3^-/\text{SO}_3^{2-}$	7.8	$2.6 \times 10^8$	(58)
$\text{SO}_5^- + \text{HSO}_3^-$	6.8	$3 \times 10^6$	(59)
$\text{H}_2\text{PO}_4^- + \text{HSO}_3^-$	4	$2.7 \times 10^8$	(59)
$\text{HPO}_4^{2-} + \text{SO}_3^{2-}$	9	$2.7 \times 10^7$	(60)
$\text{PO}_4^{3-} + \text{SO}_3^{2-}$	12	$4.1 \times 10^7$	(60)
$\text{CO}_3^{2-} + \text{SO}_3^{2-}$	11	$1 \times 10^7$	(61)
$\text{Cl}_2^- + \text{SO}_3^{2-}/\text{HSO}_3^-$	7	$3.3 \times 10^7$	(62)
$\text{Br}_2^- + \text{HSO}_3^-$	4.2	$6.9 \times 10^7$	(63)
$\text{Br}_2^- + \text{SO}_3^{2-}$	10	$2.6 \times 10^8$	(63)
$\text{I}_2^- + \text{HSO}_3^-$	3	$1.1 \times 10^6$	(63)
$\text{I}_2^- + \text{HSO}_3^-/\text{SO}_3^{2-}$	6.7	$1 \times 10^7$	(63)
$\text{I}_2^- + \text{SO}_3^{2-}$	11	$1.9 \times 10^8$	(63)
$\text{NH}_2 + \text{SO}_3^{2-}$	11	a	(63)
$\text{C}_6\text{H}_5\text{O} + \text{SO}_3^{2-}$	11	$1 \times 10^7$	(63)
$1,3\text{-HOC}_6\text{H}_4\text{O} + \text{HSO}_3^-/\text{SO}_3^{2-}$	7	$2.3 \times 10^6$	(64)
$1,3,5\text{-(HO)}_2\text{C}_6\text{H}_3\text{O} + \text{HSO}_3^{2-}/\text{SO}_3^{2-}$	7	$3.2 \times 10^6$	(64)
$\text{C}_6\text{H}_5\text{NH}_2 + \text{HSO}_3^-$	2.5	$4.8 \times 10^6$	(63)
$\text{C}_6\text{H}_5\text{NH}_2^+ + \text{SO}_3^{2-}$	b	$4 \times 10^9$	(63)
$\text{C}_6\text{H}_5\text{NH} + \text{SO}_3^{2-}$	13	$< 3 \times 10^4$	(63)
$\text{C}_6\text{H}_5\text{N(CH}_3)_3 + \text{SO}_3^{2-}$	3.6	$< 8 \times 10^5$	(63)
$\text{C}_6\text{H}_5\text{N(CH}_3)_2^+ + \text{SO}_3^{2-}$	10.9	$9.9 \times 10^8$	(63)
(chlorpromazine) $^+$ + $\text{HSO}_3^-$	3.6	$\sim 5 \times 10^5$	(59)
(promethazine) $^+$ + $\text{HSO}_3^-$	3.6	$6 \times 10^6$	(59)
(promethazine) $^+$ + $\text{HSO}_3^-/\text{SO}_3^{2-}$	6.6	$1.2 \times 10^8$	(59)
(tryptophan) $^+$ + $\text{HSO}_3^-$	3.2	$4.2 \times 10^6$	(65)
(tryptamine) $^+$ + $\text{HSO}_3^-$	3	$7.8 \times 10^6$	(65)
(tryptophanamide) $^+$ + $\text{HSO}_3^-$	3	$2.2 \times 10^7$	(65)
(iodole) $^+$ + $\text{HSO}_3^-$	3	$4 \times 10^7$	(65)
(cystine) $^+$ + $\text{HSO}_3^-/\text{SO}_3^{2-}$	7.4	$5.4 \times 10^7$	(66)

<sup>a</sup> No reaction detected ( $k < 10^5 M^{-1} \text{sec}^{-1}$ ). The redox potentials for  $\text{NH}_2$  and  $\text{SO}_3^-$  radicals appear to be very similar, judging from rate constants for their reactions with several reactants.

<sup>b</sup> Calculated from the pH dependence of the rate constant.

constants derived for the primary step, the one electron oxidation of sulfite. Bisulfite and  $\text{SO}_2\text{aq}$  are assumed to be unreactive and the reported values depend upon the acid dissociation constants chosen. Some values reported are given in Table 2.

There is no information on the oxidation by free radicals of  $\text{SO}_2\text{aq}$ , the form of sulfite present in strong acid.  $\text{Mn(III)}$ , a strong oxidant ( $E \approx 1.4 \text{ V}$ ), does react with  $\text{S(IV)}$  in 2–6  $M \text{ HClO}_4$ . The very strong inverse dependence of the rate constant on the acid concentration was interpreted as showing that bisulfite was the important reactant, not  $\text{SO}_2 \cdot \text{aq}$  (68).

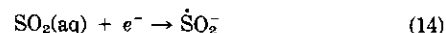
## One-Electron Reduction of S(IV)

Although not of importance in autoxidation, the reduction of  $\text{S(IV)}$  could be important in some biological systems. The hydrated electron is unreactive toward  $\text{SO}_3^{2-}$  ( $k < 10^6 M^{-1} \text{sec}^{-1}$ ) and reacts very slowly with  $\text{HSO}_3^-$  to produce hydrogen atoms ( $k = 2 \times 10^7 M^{-1} \text{sec}^{-1}$ ) (3). On the other hand,  $\text{SO}_2$  is reported

Table 2. Rate constants for the oxidation of  $\text{SO}_3^{2-}$  by complexed metal ions.

Oxidant	$k$ , $M^{-1} \text{sec}^{-1}$	Reference
$\text{Fe(CN)}_6^{3-}$	0.96	(69)
$\text{Fe(phen)}^{3+}$	$4.6 \times 10^6$	(70)
$\text{Fe(bpy)}^{3+}$	$2.1 \times 10^8$	(71)
$\text{IrCl}_6^{2-}$	$5.6 \times 10^4$	(71)
$\text{IrBr}_6^{2-}$	$3.2 \times 10^5$	(71)
$^*\text{Ru(bpy)}_3^{2+}$	$3 \times 10^5$	(72)
$\text{Ru(bpy)}_3^{3+}$	$2.2 \times 10^9$	(72)
$\text{Os(bpy)}_3^{3+}$	$9 \times 10^3$	(72)
$\text{Cu(tetraglycine)}^-$	$3.7 \times 10^4$	(73)
$\text{Mo(CN)}_8^{3-}$	$6.2 \times 10^3$	(74)
$\text{W(CN)}_8^{3-}$	22.3	(74)

to be reduced rapidly by  $\dot{\text{C}}\text{O}_2^-$  to produce  $\dot{\text{S}}\text{O}_2^-$ , while  $\text{HSO}_3^-$  and  $\text{SO}_3^{2-}$  were unreactive (75).  $\dot{\text{S}}\text{O}_2^-$  also is produced by the reduction of bisulfite using methyl viologen radical, flavodoxins, and in a  $\text{H}_2$ /hydrogenase system (76,77). More recently, enzymatic reduction of bisulfite to  $\dot{\text{S}}\text{O}_2^-$  was demonstrated in hepatic microsomal protein and ascribed to reaction of cytochrome P-450 (78). Also  $\text{Ti}^{3+}$  was found to react with sulfite in acid solutions (pH 2–6) to produce  $\dot{\text{S}}\text{O}_2^-$  (42). All the above reactions probably occur by electron transfer to  $\text{SO}_2$  rather than bisulfite. The radical  $\dot{\text{S}}\text{O}_2^-$  produced in these processes is in equilibrium with dithionite ( $\text{S}_2\text{O}_4^{2-}$ ) and is known to be a highly reactive one-electron reductant. It reduces metalloporphyrins containing  $\text{Fe(III)}$ ,  $\text{Co(III)}$ , and  $\text{Mn(III)}$  (79–81) and a wide variety of electron-transfer proteins (82). The reactivity of  $\dot{\text{S}}\text{O}_2^-$  appears to follow the same pattern as  $\dot{\text{O}}_2^-$ , with rate constants about  $10^3$  times higher (83). The potential for the process



has been estimated as  $-0.26 \text{ V}$  (84).

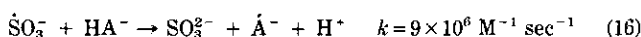
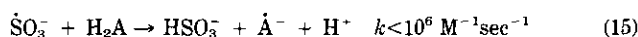
## Reactions of Sulfite Radicals

The  $\dot{\text{S}}\text{O}_3^-$  radical is for the most part a sulfur-centered radical which can act as an oxidant or reductant and like most other radicals may engage in hydrogen abstraction or addition to double bonds. Hydrogen abstraction, e.g., from isopropanol, was found to be unimportant ( $k \leq 10^3 M^{-1} \text{sec}^{-1}$ ) (3). This finding is not surprising, since the S-H bond expected to be formed in this process is much weaker than the C-H bond. (Formation of an O-H bond on sulfite is not likely due to the low spin density on the oxygens of this radical) (56).

Addition of sulfite radicals to unsaturated bonds ( $\text{C}=\text{C}$ ,  $\text{C}=\text{N}$ , and  $\text{C}\equiv\text{C}$ ) has been demonstrated by ESR (39–42,49,55). These reactions were found to be very sensitive to steric effects by substituents on the unsaturated bond. Because of the steady-state nature of these ESR experiments no kinetic data are available. Attempts to measure addition rate constants by pulse radiolysis using allyl alcohol as an example gave only

an upper limit of  $10^6 \text{ M}^{-1} \text{ sec}^{-1}$  (66). The ESR results demonstrate, however, the feasibility of sulfite radical addition to unsaturated biological targets.

Extensive kinetic studies were carried out by pulse radiolysis on the oxidation of organic substrates by  $\text{SO}_3^-$ . The results are summarized in Table 3. The sulfite radical is found to oxidize ascorbate, trolox (a water-soluble tocopherol derivative), methoxyphenol, hydroquinone, phenylenediamines, and chlorpromazine with moderate rate constants varying in the range of  $10^6$  to  $10^9 \text{ M}^{-1} \text{ sec}^{-1}$ , depending on the redox potential of the substrate and on the pH, for example with ascorbate



For hydroquinone, catechol, and several other di- and trihydroxybenzenes, the effect of pH on their reactivity with  $\text{SO}_3^-$  was demonstrated in detail (64). All of these compounds were unreactive in neutral solutions but became highly reactive as they deprotonated in basic solutions. Compared to other oxidizing radicals such as  $\text{Br}_2^-$ ,  $\text{I}_2^-$  (86), and phenoxyl (87),  $\text{SO}_3^-$  reacts more slowly and appears to be a milder oxidant. From a redox equilibrium established between bisulfite and chlorpromazine at pH 3.6 [Eq.(18)],



the redox potential for the couple  $\dot{\text{SO}}_3^-/\text{HSO}_3^-$  was measured to be 0.84V vs. NHE (59). The redox potential for the  $\text{SO}_3^{2-}/\text{SO}_3^{2-}$  couple in basic solutions is calculated (from the  $\text{pK}_a$  of  $\text{HSO}_3^- \rightleftharpoons \text{SO}_3^{2-} + \text{H}^+$ ) to be 0.63 V vs. NHE. This change in potential explains why  $\text{SO}_3^{2-}$  is oxidized by the same oxidant more readily than  $\text{HSO}_3^-$ , as discussed above (Table 1).

Since the  $\text{SO}_3^-/\text{SO}_3^{2-}$  potential is now known, reactions of  $\dot{\text{SO}}_3^-$  can be used to determine the potential for the one-electron oxidation of other species, in those cases where the electron transfer reaction is fast enough so that the decay of  $\dot{\text{SO}}_3^-$  due to self-reaction is not important. This was initially carried out for phenol (59), leading to a new value of its one-electron redox potential. More recently, equilibrium constants also have been measured for the reactions of  $\dot{\text{SO}}_3^-$  with tryptophan, tryptamine, and tryptophanamide (65), and dimethylaniline (63).

Knowing the redox potential for the reduction of  $\dot{\text{SO}}_3^-$  allows us to calculate its oxidation potential from the known two-electron redox potential for  $\text{SO}_3^{2-}$  in basic solution:

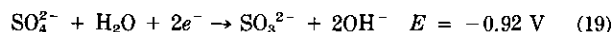


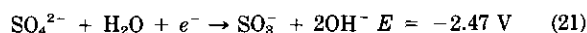
Table 3. Rate constants for reactions of  $\dot{\text{SO}}_3^-$  radicals with various reactants.

Reactant	pH	$k, \text{M}^{-1} \text{sec}^{-1}$	Reference
Ascorbic acid	<3	$<10^6$	(85)
Ascorbate ion	5-10	$9 \times 10^6$	(85)
Ascorbate dianion	>12	$3 \times 10^8$	(85)
Trolox	9	$\sim 10^6$	(85)
Phenol	11.1	$6 \times 10^{5a}$	(59)
<i>p</i> -Methoxyphenol	9.2	$4 \times 10^7$	(59)
<i>p</i> -Methoxyphenol	12.4	$1.2 \times 10^8$	(59)
Hydroquinone	7	$<10^6$	(64)
Hydroquinone	8.9	$4.5 \times 10^6$	(64)
Hydroquinone	10.5	$5.4 \times 10^7$	(64)
Hydroquinone	12.9	$3.2 \times 10^8$	(64)
Resorcinol	12.5	$1.5 \times 10^8$	(64)
<i>p</i> -Phenylenediamine	3.4	$<5 \times 10^6$	(63)
<i>p</i> -Phenylenediamine	5.3	$4.2 \times 10^6$	(63)
<i>p</i> -Phenylenediamine	9.3	$5.0 \times 10^7$	(63)
<i>N,N,N',N'</i> -Tetramethyl- <i>p</i> -phenylenediamine	4.5	$8.2 \times 10^6$	(63)
<i>N,N,N',N'</i> -Tetramethyl- <i>p</i> -phenylenediamine	9.5	$5.2 \times 10^8$	(63)
Tryptophan	3.2	$\sim 8 \times 10^{4a}$	(65)
Tryptamine	3	$5 \times 10^{4a}$	(65)
Tryptophanamide	3	$4 \times 10^{5a}$	(65)
Chlorpromazine	3.6	$\sim 5 \times 10^{6a}$	(59)
$\text{O}_2$	6.8	$1.5 \times 10^9$	(59)
Lipoic acid	7,12	NR <sup>b</sup>	(64)
<i>N</i> -Methylisonicotinic acid	7	NR	(64)
Anthraquinone-2-sulfonate	7	NR	(64)
Histidine	7	NR	(64)
Allyl alcohol	7	NR	(64)

<sup>a</sup> Reaction leads to equilibrium; see back reaction in Table 1.

<sup>b</sup> No reaction detected by pulse radiolysis, indicating usually  $k < 10^5 \text{ M}^{-1} \text{ sec}^{-1}$ .

Subtracting  $E(\dot{\text{SO}}_3^-) = 0.63 \text{ V}$  from twice the former value ( $-0.92 \text{ V}$ ) leads to



This suggests that  $\dot{\text{SO}}_3^-$  can act as both a mild oxidant or a strong reductant. It may be difficult to demonstrate the reducing power of  $\text{SO}_3^-$  since many oxidants will react with sulfite ions before the  $\dot{\text{SO}}_3^-$  radicals are produced in the radiolysis. Moreover, the above calculation of redox potential may not reflect the actual reducing power of  $\text{SO}_3^-$  since the initial product is  $\text{SO}_3$ , which is subsequently hydrated to  $\text{SO}_4^{2-}$ , possibly much more slowly than the electron transfer (as argued for the case of  $\text{SO}_2^-$ ) (84). In addition, it has been argued on the basis of spin density on the sulfur, that  $\dot{\text{SO}}_3^-$  is a much weaker reductant than  $\dot{\text{SO}}_2^-$  (55).

Biological damage by  $\text{SO}_3^-$  may be partly due to oxidation reactions similar to those in Table 3. But the main harmful effects of this radical may lie in the fact that it reacts very rapidly with  $\text{O}_2$ ,  $k = 1.5 \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}$ , to form a peroxy radical which is much more reactive.



The alternative reaction path forming  $\text{SO}_3 + \text{O}_2^-$  was

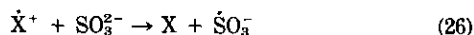
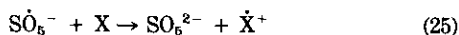
found (85) to be unimportant, at least under the experimental conditions of pH 3–12.

## Reactions of Peroxysulfate Radical

The  $\dot{\text{S}}\text{O}_5^-$  radical is a stronger oxidant than  $\dot{\text{S}}\text{O}_3^-$ ; its one-electron redox potential is estimated to be about 1.1 V at pH 7 (59). Table 4 indeed shows that  $\dot{\text{S}}\text{O}_5^-$  oxidizes several substrates considerably more rapidly than  $\text{SO}_3^-$ , e.g., with ascorbate



Moreover, it can oxidize certain substrates (aniline and dimethylaniline, for example) which are not attacked by  $\text{SO}_3^-$  at all and which, in fact, can form radicals that oxidize sulfite ions. In such cases, when the redox potential of the substrate is intermediate between those of  $\text{SO}_3^-$  and  $\text{SO}_5^-$ , a chain reaction is likely to develop in the presence of  $\text{O}_2$  following the general pattern shown in eqs. (24)–(26).

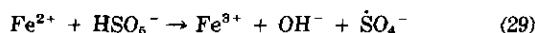
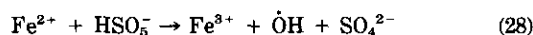


Although  $\dot{\text{S}}\text{O}_5^-$  can oxidize directly sulfite or bisulfite ions, the intermediacy of a substrate X may enhance the chain process of sulfite oxidation (or peroxidation) by oxygen.

The one-electron reduction of  $\text{SO}_5^-$  yields  $\text{HSO}_5^-$ , peroxymonosulfate (Caro's acid). This is a strong oxidant, with a standard two-electron reduction potential of 1.82 V (88).



Peroxymonosulfate is known to oxidize many organic compounds (89). Of considerable interest is its ability to oxidize sulfides to sulfones (90) and primary aryl amines to nitroso compounds (91). In addition to these reactions with organic compounds, which might involve oxygen atom transfer, peroxymonosulfate can be reduced by metal ions, possibly producing the highly reactive free radicals,  $\text{SO}_4^-$  or  $\text{OH}$ , as it does upon reaction with  $e_{\text{aq}}^-$  (92), e.g.



These radicals, in turn, are capable of rather indiscriminate attack on biological molecules.

The  $\text{SO}_5^-$  radical possibly can also react by atom transfer. This mechanism has been proposed for its reaction with bisulfite (30).

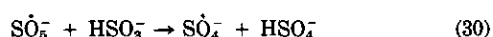


Table 4. Comparison of some rate constants for reactions of  $\dot{\text{S}}\text{O}_3^-$ ,  $\dot{\text{S}}\text{O}_5^-$  and  $\dot{\text{S}}\text{O}_4^-$  with organic compounds.

Compound	Rate constants, $\text{M}^{-1} \text{sec}^{-1}$		
	$\text{SO}_3^-$	$\text{SO}_5^-$	$\text{SO}_4^-$
Ascorbic	$<10^6$	$2 \times 10^{6a}$	b
Ascorbate	$9 \times 10^6$	$1.4 \times 10^{6a}$	b
Trolox	$\sim 10^6$	$1.2 \times 10^{7a}$	b
Hydroquinone	$<10^6$	$2.7 \times 10^6$	b
Hydroquinone-monoanion	$5 \times 10^7$		b
Catechol	$<10^6$	$2.7 \times 10^6$	b
Resorcinol	(reverse)	$<1 \times 10^6$	b
Aniline	(reverse)	$3 \times 10^{6c}$	b
N,N-Dimethylaniline	(reverse)	$1 \times 10^{7c}$	b
Tyrosine	$<10^6$		$\sim 3 \times 10^{9d}$
Tryptophan	$8 \times 10^4$		$\sim 2 \times 10^{9d}$
Histidine	NR		$\sim 2.5 \times 10^{9d}$
i-PrOH	$<10^3$		$\sim 8 \times 10^{7d}$
Ethanol		$<10^{3e}$	$\sim 3 \times 10^{7d}$
Fumarate	$<10^5$		$\sim 2 \times 10^{7d}$
Allyl alcohol	NR		$1.5 \times 10^{9d}$
Glycine	$<10^3$		$\sim 9 \times 10^{6d}$
$\text{HSO}_3^-$	—	$3 \times 10^{6f}$	$\sim 10^{9d}$

<sup>a</sup> Data of Huie and Neta (85).

<sup>b</sup> Was not measured because of thermal reaction of the substrate with  $\text{S}_2\text{O}_8^{2-}$ , the precursor of  $\text{SO}_4^-$ . The reaction, however, is expected to be very fast ( $k \geq 10^9 \text{ M}^{-1}\text{sec}^{-1}$ ).

<sup>c</sup> Data of Neta and Huie (63).

<sup>d</sup> From Ross and Neta (86).

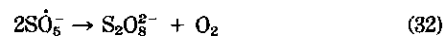
<sup>e</sup> Data of Hayon et al. (3).

<sup>f</sup> Data of Huie and Neta (59).

Other reactions of bisulfite are known to involve oxygen atom transfer (93–97).

If  $\dot{\text{S}}\text{O}_5^-$  is capable of transferring an oxygen atom, the direct oxygenation of organic compounds is feasible, possibly producing the  $\dot{\text{S}}\text{O}_4^-$  radical as a by product. The existence of this type of reaction has not been confirmed.

The mechanism of the self-reaction of  $\dot{\text{S}}\text{O}_5^-$  is not known. It has been proposed that the reaction leads to stable products and serves to terminate the autoxidation of sulfite (11). On the other hand, the reaction has been proposed to go to  $\dot{\text{S}}\text{O}_4^-$  or  $\text{S}_2\text{O}_8^{2-}$  (98).



with the ratio  $k(\dot{\text{S}}\text{O}_4^{2-})/k(\text{S}_2\text{O}_8^{2-}) = 9$ . Although this reaction is not likely to be important in the physiological role of sulfite, it could be important in some of the laboratory studies of the effects of sulfite oxidation on biological systems. The mechanism of this reaction certainly deserves more study.

## Reactions of Sulfate Radical

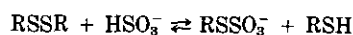
The  $\dot{\text{S}}\text{O}_4^-$  radical, possibly produced by the reactions discussed above, is very reactive toward organic compounds. It can abstract H atoms, add to double bonds,

and oxidize by electron transfer quite rapidly. The rate constants for such reactions with many organic compounds are summarized in a recent compilation (86) (see examples in Table 4) and will not be discussed here. It is clear, however, that  $\text{SO}_4^-$  attacks biological targets indiscriminately.

## Conclusions

It has been apparent for some time that the effects of  $\text{SO}_2$  autoxidation on organic and biological systems are due to reactive intermediates. Since the reactivities of many of these intermediates are now known, the mechanism of these effects can be better understood. For several of the organic compounds, like hydroquinone and other phenolic species, reaction with  $\text{SO}_3^-$  and  $\text{SO}_5^-$  is possible. Indeed, they prove to be the most efficient inhibitors of  $\text{SO}_2$  autoxidation. For other organic compounds, like mannitol and methionine, only reactions with  $\text{SO}_4^-$  are likely. Production of  $\text{HSO}_5^-$  from the reduction of  $\text{SO}_5^-$  opens up additional possibilities, including direct reaction of  $\text{HSO}_5^-$  and its decomposition to produce  $\text{SO}_4^-$  or  $\text{OH}$ .

Within the body, it is apparent that if  $\text{SO}_2$  is allowed to undergo autoxidation, cellular damage is inevitable. Whether the presence of S(IV) beyond the region of the lungs can lead to similar damage is not apparent. To a large extent this damage will depend on the equilibrium



and the probability of forming radicals from  $\text{RSSO}_3^-$ . One-electron reduction of this compound is expected to yield  $\text{SO}_3^-$  radicals. This was recently supported by pulse radiolysis experiments, whereby reduction of  $\text{RSSO}_3^-$  by  $e_{\text{aq}}^-$  and  $(\text{CH}_3)_2\text{COH}$  was found to form a radical which oxidized ascorbate with the same rate constant as does  $\text{SO}_3^-$  (66). If reduction of  $\text{RSSO}_3^-$  to  $\text{SO}_3^-$  radical occurs with biological reductants, this could lead to oxidative damage by the  $\text{SO}_3^-$  and the other radicals produced from it. Thus the RS group serves not only as a carrier of sulfite but it also changes the requirements for  $\text{SO}_3^-$  radical formation from oxidation to reduction.

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## REFERENCES

- Altshuler, A. P. (Ed.) The Acidic Deposition Phenomenon and its Effects. Critical Assessment Review Papers, Vol. 1 Public Review Draft, EPA EPA-600/8-83-016A, 1983.
- Huss, A., and Eckert, C. A. Equilibria and ion activities in aqueous sulfur dioxide solutions. *J. Phys. Chem.* 81: 2268-2270 (1977).
- Hayon, E., Treinin, A., and Wilf, J. Electronic spectra, photochemistry, and autoxidation mechanism of the sulfite-bisulfite-pyrosulfite systems, the  $\text{SO}_2^-$ ,  $\text{SO}_3^-$ ,  $\text{SO}_4^-$ , and  $\text{SO}_5^-$  radicals. *J. Am. Chem. Soc.* 94: 47-57 (1972).
- Connick, R. E., Tam, T. M., and von Deuster, E. Equilibrium constant for the dimerization of bisulfite ion to form  $\text{S}_2\text{O}_5^{2-}$ . *Inorg. Chem.* 21: 103-107 (1982).
- Kleinman, M. T. Sulfur dioxide and exercise: relationship between response and absorption in upper airways. *J. Air. Poll. Control Assoc.* 34: 32-37 (1984).
- Schachter, E. N., Witek, T. J., Beck, G. J., Hosein, H. R., Colice, G., Leaderen, B. P., and Cain, W. Airway effects of low concentrations of sulfur dioxide: dose-response characteristics. *Arch. Environ. Health* 39: 34-42 (1984).
- Rajagopalan, K. V., and Johnson, J. L., Biological origin and metabolism of  $\text{SO}_2$ . In: *Biochemical Effects of Environmental Pollutants* (S. D. Lee, Ed.), Ann Arbor Science, Ann Arbor, MI 1977, pp. 307-314.
- Petering, D. H. Sulfur dioxide: a view of its reactions with biomolecules. In: *Biochemical Effects of Environmental Pollutants* (S. D. Lee, Ed.), Ann Arbor Science, Ann Arbor, MI, 1977, pp. 293-306.
- Stricks, W., and Kolthoff, I. M. Equilibrium constants of the reactions of sulfite with cystine and with dithiodiglycolic acid. *J. Am. Chem. Soc.* 73: 4569-4574 (1951).
- Sies, H., Brigelilius, R., and Akerboom, T. P. M. Intrahepatic glutathione status, In: *Functions of Glutathione. Biochemical, Physiological, Toxicological, and Clinical Aspects* (A. Larsson, S. Orrenius, A. Holmgren, and B. Mamervik, Eds.), Raven Press, New York, 1983, pp. 51-64.
- Huie, R. E., and Peterson, N. C., Reactions of sulfur(IV) with transition-metal ions in aqueous solutions. In: *Trace Atmospheric Constituents: Properties, Transformations, and Fates* (S. E. Schwartz, Ed.), John Wiley & Sons, New York, 1983, pp. 117-146.
- Hoffmann, M. R., and Boyce, S. D. Catalytic autoxidation of aqueous sulfur dioxide in relationship to atmospheric systems, In: *Trace Atmospheric Constituents: Properties, Transformations, and Fates* (S. E. Schwartz, Ed.), John Wiley & Sons, New York, 1983, pp. 147-189.
- Bigelow, S. L. Katalytische Wirkungen auf die Geschwindigkeit der Oxidation des Natriumsulfits durch den Sauerstoff der Luft. *Z. Physik. Chem.* 28: 493-532 (1898).
- Young, S. W. On the inhibition of chemical reactions by foreign substances. 1. *J. Am. Chem. Soc.* 24: 297-327 (1902);
- Dev, B. and Jain, B. D. Inhibitors of the autoxidation of sodium sulphite solutions. *J. Sci. Ind. Res.* 20D: 461-462 (1961).
- Mathews, J. H., and Weeks, M. E. The effect of various substances on the photochemical oxidation of solutions of sodium sulfite. *J. Am. Chem. Soc.* 39: 635-640 (1917).
- Alyea, H. N., and Backstrom, H. L. J. The inhibitive action of alcohols on the oxidation of sodium sulfite. *J. Am. Chem. Soc.* 51: 90-109 (1929).
- Kharasch, M. S., May, E. M., and Mayo, F. R., The peroxide effect in the addition of reagents to unsaturated compounds. XVIII. The addition and substitution of bisulfite. *J. Org. Chem.* 3: 175-192 (1938).
- Baumgarten, P., and Erbe, H. Mechanismen der Sulfite-Oxydation. III. Mitteil. Über die Oxydation wässriger Sulfite-Lösungen. *Ber. Deut. Chem. Ges.* B70: 2235-2264 (1937).
- LuValle, J. E. The reaction of quinone and sulfite. I. Intermediates. *J. Am. Chem. Soc.* 74: 2970-2977 (1952).
- Lim, P. K., Huss, A., and Eckert, C. A. Oxidation of aqueous sulfur dioxide. 3. The effects of chelating agents and phenolic antioxidants. *J. Phys. Chem.* 86: 4233-4237 (1982).
- Berkely, H. B. *Phot. News* 26: 41 (1882).
- Fridovich, I., and Handler, P. Detection of free radicals generated during enzymatic oxidations by the initiation of sulfite oxidation, *J. Biol. Chem.* 236: 1836-1840 (1961).
- Fridovich, I., and Handler, P. Xanthine oxidase III. Sulfite oxidation as an ultra sensitive assay. *J. Biol. Chem.* 233: 1578-1580 (1958).
- Klebanoff, S. J. The sulfite-activated oxidation of reduced pyridine nucleotides by peroxidase. *Biochem. Biophys. Acta* 48: 93-103 (1961).
- Chen, W. W. L. A method for the complete sulfonation of cysteine residues in proteins. *Biochemistry* 7: 4247-4254 (1968).
- Hayatsu, H. The oxygen catalyzed reaction between 4-thiouridine and sodium sulfite. *J. Am. Chem. Soc.* 91: 5693-5694 (1969).



28. Hayatsu, H. and Inoue, M. The oxygen-mediated reaction between 4-thiouracil derivatives and bisulfite. Isolation and characterization of 1-methyluracil 4-thiosulfate as an intermediate in the formation of 1-methyluracil-4-sulfonate. *J. Am. Chem. Soc.* 93: 2301-2306 (1971).
29. Yang, S. F. Sulfoxide formation from methionine or its sulfite analogs during aerobic oxidation of sulfite. *Biochemistry* 9: 5008-5014 (1970).
30. Hayatsu, H., and Miller, R. C. The cleavage of DNA by the oxygen dependent reaction of bisulfite. *Biochem. Biophys. Res. Commun.* 46: 120-124 (1972).
31. Yang, S. F., and Saleh, M. A. *Phytochemistry*, 12: 1463 (1973).
32. Yang, S. F. Destruction of tryptophan during the aerobic oxidation of sulfite ions. *Environ. Res.* 6: 395-402 (1973).
33. Hayatsu, H. *Progr. Nucleic Acid Res. Mol. Biol.* 16: 75 (1976).
34. Kaplan, D., McIlton, C., and Luchtel, D. Bisulfite induced lipid oxidation. *Arch. Environ. Health* 30: 507-509 (1975).
35. Inouye, B., Ikeda, M., Ishida, T., Ogata, M., Akiyama, J., and Utsumi, K. Participation of superoxide free radical and  $Mn^{2+}$  in sulfite oxidation. *Toxicol. Appl. Pharmacol.* 46: 29-38 (1978).
36. Peiser, G. D., and Yang, S. F. *J. Agr. Food Chem.* 27: 446 (1979).
37. Jaroensanti, J., Panjipun, B., and Intern, J. J. *Vit. Nutr. Res.* 51: 34 (1961).
38. Fujimoto, S., Nakagawa, T., Ishimitsu, S., and Ohara, A. On the mechanism of inactivation of papain by bisulfite. *Chem. Pharm. Bull.* 31: 992-1000 (1983).
39. Ozawa, T., Setaka, M., and Kwan, T. ESR studies of the sulfite radical anion. *Bull. Chem. Soc. Japan* 44: 3473-3474 (1971).
40. Ozawa, T., Setaka, M., Yamamoto, H., and Kwan, T. On the reaction of the sulfite radical anions with thioureas. *Chem. Pharm. Bull.* 22: 962-964 (1974).
41. Ozawa, T., and Kwan, T. ESR evidence for the formation of new vinyl radicals in solution. *J. Chem. Soc. Chem. Commun.* 1983: 80-81 (1983).
42. Norman, R. O. C., and Storey, P. M. Electron spin resonance studies. Part XXXI. The generation, and some reactions, of the radicals  $SO_3^-$ ,  $S_2O_3^-$ ,  $S^-$ , and  $SH$  in aqueous solution. *J. Chem. Soc. B* 1971: 1009-1012.
43. Zagorski, Z. P., Sehested, K., and Nielsen, S. O. Pulse radiolysis of aqueous alkaline sulfite solutions. *J. Phys. Chem.* 75: 3510-3517 (1971).
44. Eriksen, T. E. pH effect on the pulse radiolysis of deoxygenated aqueous solutions of sulfur dioxide. *J. Chem. Soc. Faraday Trans I* 70: 208-215 (1974).
45. Sadat-Shafai, T., Pucheault, J., and Ferradini, C. A radiolysis study of the role of superoxide ion in the oxidation of sulfite by oxygen. *Radiat. Phys. Chem.* 17: 283-288 (1981).
46. Behar, D., and Fessenden, R. W. Electron spin resonance studies of inorganic radicals in irradiated aqueous solutions. I. Direct observation. II. Radical trapping with nitromethane. *J. Phys. Chem.* 76: 1706-1721 (1972).
47. Verma, N. C., and Fessenden, R. W. Time resolved ESR spectroscopy. IV. Detailed measurement and analysis of the ESR time profile. *J. Chem. Phys.* 65: 2133-2155 (1976).
48. Dogliotti, L., and Hayon, E. Flash photolysis study of sulfite, thiocyanate, and thiosulfate ions in solution. *J. Phys. Chem.* 72: 1800-1807 (1968).
49. Chawla, O. P., Arthur, N. L., and Fessenden, R. W. An electron spin resonance study of the photolysis of aqueous sulfite solutions. *J. Phys. Chem.* 77: 772-776 (1973).
50. Dogliotti, L., and Hayon, E. Optical spectrum of  $SO_3^-$  radicals produced from the photolysis of dithionate ions in solution. *Nature* 218: 949-950 (1968).
51. Behar, D., and Fessenden, R. W. An investigation of radicals produced in the photolysis of thiosulfate solutions by electron spin resonance. *J. Phys. Chem.* 75: 2752-2755 (1971).
52. Mottley, C., Trice, T. B., and Mason, R. P. Direct detection of the sulfur trioxide radical anion during the horseradish peroxidase-hydrogen peroxide oxidation of sulfite (aqueous sulfur dioxide). *Mol. Pharmacol.* 22: 732-737 (1982).
53. Mottley, C., Mason, R. P., Chignell, L. F., Sivarejah, K., and Eling, T. S. The formation of sulfur trioxide radical anion during the prostaglandin hydroperoxidase-catalyzed oxidation of bisulfite (hydrated sulfur dioxide). *J. Biol. Chem.* 257: 5050-5055 (1982).
54. Fessenden, R. W. Private communication.
55. Ozawa, T., and Kwan, T. ESR studies on the reactive character of the radical anions  $SO_3^-$ ,  $SO_3^{\cdot-}$ , and  $SO_4^{\cdot-}$  in aqueous solution. *Polyhedron* 2: 1019-1023 (1983).
56. Chantry, G. W., Horsfield, A., Morton, J. R., Rowlands, J. R., and Whiffen, D. H. The optical and electron spin resonance spectra of  $SO_3^-$ . *Mol. Phys.* 5: 233-239 (1962).
57. Adams, G. E., and Boag, J. W. Spectroscopic studies of reactions of the OH radical. *Proc. Chem. Soc.* 1964: 112.
58. Chawla, O. P. An electron spin resonance study of the mechanism and kinetics of photochemical reactions in aqueous solutions. Ph.D. Thesis, Carnegie-Mellon University, Pittsburgh, PA, 1973.
59. Huie, R. E., and Neta, P. The chemical behavior of  $SO_3^-$  and  $SO_3^{\cdot-}$  radicals in aqueous solutions. *J. Phys. Chem.* 88: 5665-5669 (1984).
60. Maruthamuthu, P., and Neta, P. Phosphate radicals. Spectra, acid-base equilibria, and reactions with inorganic compounds. *J. Phys. Chem.* 82: 710-713 (1978).
61. Lilie, J., Henglein, A., and Hanrahan, R. J.  $O^-$  transfer reactions of the carbonate radical anion. *Radiat. Phys. Chem.* 11: 225-227 (1978).
62. Hasegawa, K., and Neta, P. Rate constants and mechanisms of reaction of  $Cl_2^-$  radicals. *J. Phys. Chem.*, 82: 854-857 (1978).
63. Neta, P., and Huie, R. E. One electron redox reactions involving sulfite ions and aromatic amines. *J. Phys. Chem.* 89: 1783-1787 (1985).
64. Huie, R. E., and Neta, P. One-electron redox reactions in aqueous solutions of sulfite with hydroquinone and other hydroxyphenols. *J. Phys. Chem.* in press.
65. Jovanovic, S. and Simic, M. G. *Rad. Phys. Chem.*, submitted.
66. Huie, R. E., and Neta, P. Unpublished results.
67. West, P. W., and Gaeke, G. C. Fixation of sulfur dioxide as disulfite-mercurate(II) and subsequent colorimetric estimation. *Anal. Chem.* 28: 1816-1819 (1956).
68. Siskos, P. A., Peterson, N. C., and Huie, R. E. Kinetics of the manganese(III)-sulfur(IV) reaction in aqueous perchloric acid solutions. *Inorg. Chem.* 23: 1134-1137 (1984).
69. Murray, R. S. Reinvestigation of the reaction between hexacyanoferrate(III) and sulphite ions. *J. Chem. Soc. Dalton Trans.* 22: 2381-2383 (1974).
70. Carlyle, D. W. Electron transfer between sulfur(IV) and tris(1,10-phenanthroline)iron(III) ion in aqueous solution. *J. Am. Chem. Soc.* 94: 4525-4529 (1972).
71. Wilmarth, W. K., Stanbury, D. M., Byrd, J. E., Po, H. N., and Chua, C. P. Electron-transfer reactions involving simple free radicals. *Coord. Chem. Revs.* 51: 155-179 (1983).
72. Creutz, C., Sutin, N., and Brunschwig, B. S. Excited-state photochemistry in the tris(2,2'-bipyridine)ruthenium(II)-sulfite system. *J. Am. Chem. Soc.* 101: 1297-1298 (1979).
73. Anast, J. M., and Margerum, D. W. Trivalent copper catalysis of the autooxidation of sulfite. Kinetics and mechanism of the copper(III,II) tetraglycine reactions with sulfite. *Inorg. Chem.* 20: 2319-2327 (1981).
74. Dennis, C. R., Basson, S. S., and Leipoldt, J. G. Kinetics and salt effects of the reduction of octacyanomolybdate(V) and octacyanotungstate(V) by sulphite ions. *Polyhedron* 2: 1357-1362 (1983).
75. Eriksen, T. E. Pulse radiolytic investigation of the  $SO_2^-$  radical ion. *Radiochem. Radioanal. Letters* 22: 33-40 (1975).
76. Mayhew, S. G., Abels, R., and Platenkamp, R. The production of dithionite and  $SO_2^-$  by chemical reaction of (bi)sulphite with methyl viologen semiquinone. *Biochem. Biophys. Res. Commun.* 77: 1397-1403 (1977).
77. Mayhew, S. G. The redox potential of dithionite and  $SO_2^-$  from equilibrium reactions with flavodoxins, methyl viologen, and hydrogen plus hydrogenase. *Eur. J. Biochem.* 85: 535-547 (1978).
78. Mottley, C., Harman, and Mason, R. P. To be published.
79. Hambright, P., and Chock, P. B. Metal-porphyrin interactions. IV. Electron-transfer kinetics between dithionite and manganese(III) and cobalt(III) porphyrins. *Inorg. Chem.* 13: 3029-3031 (1974).



80. Worthington, P., and Hambricht, P., Kinetics of the oxidation of dithionite by dicyanoporphyrinatoferrate(III) complexes. *J. Inorg. Nucl. Chem.* 42: 1651-1654 (1980).
81. Hambricht, P., Lemelle, S., Alston, R., Neta, P., Newball, H. H., and diStefano, S. A dissociative mechanism for the dithionite reduction of cobalt(III) myoglobin. *Inorg. Chim. Acta* 92: 167-172 (1984).
82. Lambeth, D. O. and Palmer, G., The kinetics and mechanism of reduction of electron transfer proteins and other compounds of biological interest by dithionite. *J. Biol. Chem.* 248: 6095-6103 (1973).
83. Bradic, Z., and Wilkins, R. G., Comparative behavior in the kinetics of reduction of superoxide and dithionite ions, *J. Am. Chem. Soc.* 106: 2236-2239 (1984).
84. Stanbury, D. M., and Lednický, L. A. Outer-sphere electron transfer reactions involving the chlorite/chlorine dioxide couple. Activation barriers for bent triatomic species, *J. Am. Chem. Soc.* 106: 2847-2853 (1984).
85. Huie, R. E., and Neta, P. Oxidation of ascorbate and a tocopherol analogue by the sulfite derived radicals  $\text{SO}_3^-$  and  $\text{SO}_5^-$ . *Chem.-Biol. Interact.* 53: 233-238 (1985).
86. Ross, A. B., and Neta, P. Rate constants for reactions of inorganic radicals in aqueous solution, *Natl. Stand. Ref. Data Ser., Natl. Bur. Stand., Report No. 65* (1979).
87. Schuler, R. H., Oxidation of ascorbate anion by electron transfer to phenoxyl radicals. *Radiat. Res.* 69: 417-433 (1977).
88. Steele, W. V., and Appelman, E. H. The standard enthalpy of formation of peroxymonosulfate ( $\text{HSO}_5^-$ ) and the standard electrode potential of the peroxymonosulfate-bisulfate couple. *J. Chem. Thermodynamics* 14: 337-344 (1982).
89. Kennedy, R. J., and Stock, A. M. The oxidation of organic substances by potassium peroxymonosulfate. *J. Org. Chem.* 25: 1901-1906 (1960).
90. Trost, B. M., and Curran, D. P. Chemoselective oxidation of sulfides to sulfones with potassium hydrogen persulfate. *Tetrahedron Letters* 22: 1287-1290 (1981).
91. March, J. *Advanced Organic Chemistry*. McGraw-Hill, New York, 1977, p. 1109.
92. Roebke, W., Renz, M., and Henglein, A. Pulseradiolyse der Anionen  $\text{S}_2\text{O}_8^{2-}$  und  $\text{HSO}_5^-$  in waessriger Loesung. *Int. J. Radiat. Phys. Chem.* 1: 39-44 (1969).
93. Halperin, J. and Taube, H. The transfer of oxygen atoms in oxidation-reduction reactions. III. The reaction of halogenates with sulfite in aqueous solution. *J. Am. Chem. Soc.* 74: 375-380 (1952).
94. Halperin, J., and Taube, H. The transfer of oxygen atoms in oxidation-reduction reactions. IV. The reaction of hydrogen peroxide with sulfite and thiosulfate, and of oxygen, manganese dioxide and permanganate with sulfite. *J. Am. Chem. Soc.* 74: 380-382 (1952).
95. Appelman, E. V., Klaning, U. K., and Thompson, R. C. Some reactions of the perbromate ion in aqueous solution. *J. Am. Chem. Soc.* 101: 929-934 (1979).
96. Lumenok-Burmakina, V. A., and Gerasenkova, A. N., Mechanism of the oxidation of inorganic sulfur compounds by hydrogen peroxide, *Russ. J. Inorg. Chem.* 9: 149-152 (1964).
97. Lumenok-Burmakina, V. A., Aleeva, G. P., and Franchuk, T. M. Mechanism of the oxidation of inorganic oxo-anions by peroxo-mono-acids. *Russ. J. Inorg. Chem.* 13: 509-512 (1968).
98. Thompson, R. C. Catalytic decomposition of peroxymonosulfate in aqueous perchloric acid by the dual catalysts  $\text{Ag}^+$  and  $\text{S}_2\text{O}_8^{2-}$  and by  $\text{Co}^{2+}$ . *Inorg. Chem.* 20: 1005-1010 (1981).